are microprocessor-controlled, injections are precise and reproducible. The rate of flow is typically 0.5 ml min^{-1}, controlled with a 4-channel peristaltic pump which may also be placed at an outlet of the system. The analyte-containing sample S is injected into sample loop SL and sensitized liposomes L are injected into sample loop KL which is appropriately coiled or knotted to promote mixing. The immunoreactor column is typically a glass column packed with nonporous soda lime glass beads or with solid polystyrene spheres which range from 100 to several hundred micrometers in diameter and may be derivatized as described above. As the injected sample S is transported through the system, it undergoes controlled dispersion and can interact with immobilized reagent on the immunoreactor column. The sample may also be chemically and/or physically treated by the introduction of appropriate reagents or processing such as mixing with a carrier solution C and/or chaotropic agents CA. The result of this sample treatment is then quantified, preferably by using a surfactant Surf to disrupt the liposomes L, a lysis delay coil LC to promote complete disruption, and a fluorescence or electrochemical flow-through detector D to detect marker compound released by the disrupted liposomes.

The FIA configuration is readily adaptable to different immunoassay formats, including noncompetitive assays (FIG. 4 assays III–V). Adapting the system to a new analyte is straightforward since the chemistry for antibody fragment immobilization is generic. Once prepared, an immunoreactor column specific for a particular analyte is expected to be stable to storage for many months, and reusable for hundreds of assays. The system can be adapted to quantify more than one analyte simultaneously. The use of microprocessor control allows completely automated operation. FIA is a multisampling, high throughput technique based on small reaction volumes. The small volume reactor column produces rapid equilibration times for antigen-antibody reactions, in sharp contrast to the lengthy adsorption steps required for most solid-phase assays. Because reagents are immobilized, the system is reusable and expensive reagents are conserved. In addition, the ability to reuse the immunoreactor column means that the system can be calibrated with known solutions and provide quantitative information, in contrast to the qualitative or semiquantitative response of current assays.

FIG. 4 illustrates different competitive and non-competitive FIA assay schemes according to an embodiment of the present invention.

The competitive assays, schemes I and II, are based on there being a limited number of sites available for binding the antigen-derivatized liposomes and analytes to the Fab′ receptors on the immunoreactor column.

Scheme I illustrates the saturation of the reactor with both a liposome reagent and a sample. If the binding of the analyte to the reactor receptors results in fewer receptor sites available for binding than the number of derivatized liposomes in the reactor, then the number of liposomes not bound to the receptor can be related to the number of analytes bound. The concentration of analyte in the sample reagent can thus be determined by detecting the number of unbound liposomes.

Scheme II also illustrates saturating the reactor with both a liposome reagent and a sample reagent, but, unlike scheme I, the number of bound liposomes are detected and can be related to the number of analyte molecules bound to the reactor. An acid, detergent or solvent is used to wash the bound liposomes from the reactor so they can be detected and quantified.

Preferred non-competitive assays according to present invention are illustrated by schemes III–V in FIG. 4.

Scheme III represents a non-competitive assay employing liposomes derivatized with whole antibodies or the antigen-binding portion, Fab′ fragments, of antibodies in their outer membranes. An excess of derivatized liposomes is mixed with a sample, and the Fab′ portions of the liposomes react with and bind to the analytes in the sample. This mixture is then introduced into the reactor where binding of unreacted liposomes takes place. The reactor, according to this scheme, has been covalently derivatized with an appropriate binding agent, which is an analyte analog, prior to introducing the liposome-sample mixture. The liposomes not bound to sample analytes can bind to the binding agents on the reactor. Liposomes bound to sample analytes do not bind to the reactor and thus pass through the reactor and downstream where they can be collected and quantified. The number of liposomes collected is thus directly related to the number of analyte molecules in the sample.

Scheme IV is a sandwich-type assay which, like scheme III, employs liposomes derivatized with antibodies or with the Fab′ fragments of antibodies in their outer membranes. The reactor receptors are also antibodies or Fab′ fragments. Here, the sample reagent is first introduced into the reactor where binding between the analytes and the reactor receptors takes place. The reactor is then saturated with the derivatized liposomes which bind to the analytes already bound to the reactor. Remaining liposomes do not bind to the reactor receptor but are instead carried downstream. The number of liposomes bound to the reactor is thus directly proportional to the number of analyte molecules in the sample. The bound liposomes can also be liberated by washing the reactor with a regenerating agent and collecting and quantifying the markers downstream.

Scheme V of FIG. 4 is yet another non-competitive assay of the present invention. Here, the sample reagent is first introduced into the reactor where the analytes bind to the reactor receptors. Then, liposomes sensitized with antigens in their outer membranes are introduced into the reactor where they bind to the remaining unbound reactor receptor sites. The difference between the number of liposomes not bound and the number of liposomes introduced into the reactor is related to the number of reactor receptor sites not bound to analyte molecules. Alternatively, the reactor column can be washed with a regenerating agent to free the liposome marker molecules so they can be collected and quantified downstream. The number of marker molecules can be related to the number of analyte molecules bound to the reactor.

This invention is useful for quantification of analytes which could be antigens or antibodies, such as might be found in clinical samples or in large scale fermentation reactions. Operation modes include sequential automated injection of specimens, or on-line monitoring at designated time intervals. It could be used as well for quantification of particulate infectious agents such as viruses and bacteria, and for detection and separation of cells according to their surface antigens. Continuous effluent stream monitoring is also possible with few modifications to the current design.